Center for Biologics Evaluation and Research Update

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History of Biological Products Regulation

1798 Marine Hospital Service Original Public Health Agency

1800 Smallpox Vaccination

1850 Louis Pasteur (Rabies Vaccine)

1878 Koch Isolated Anthrax Bacillus

1886 Heat-Killed Vaccines

1887 Public Service Lab of Hygiene J. Kinyoun

1888 Roux/ Yersin (Diphtheria Toxin)

1890 Antitoxins

1894 PHS Lab Produces Diphtheria Antitoxin

1901 13 Children Died of Tetanus from Contaminated Diphtheria Antitoxin

1902 Biologics Control Act

History of Biological Products Regulation (continued)

1906 The Food and Drug Act

1912 Public Health Service

1930 National Institute of Health

1937 Division of Biologics Control

1938 Food and Drug Cosmetic Act Section 505

1940 Rh Blood Group System

1941 Cohn Fractionation of Blood

1944 The Public Health Service Act (Lab of Biologics Control)

1948 National Microbiological Institute

1950 1st Live Polio Vaccine in Humans

History of Biological Products Regulation (continued)

1955 — Cutter Polio Vaccine Incident

1955 — Division of Biologics Standards (DBS) (NIH)

1962 — Kefauver-Harris Drug Amendment

1972 — DBS To FDA, Became Bureau of Biologics

1973 — New Provisions of PHS Act

1974 — National Blood Policy

1980's — Biotechnology Era

1982 — National Center for Drugs and Biologics

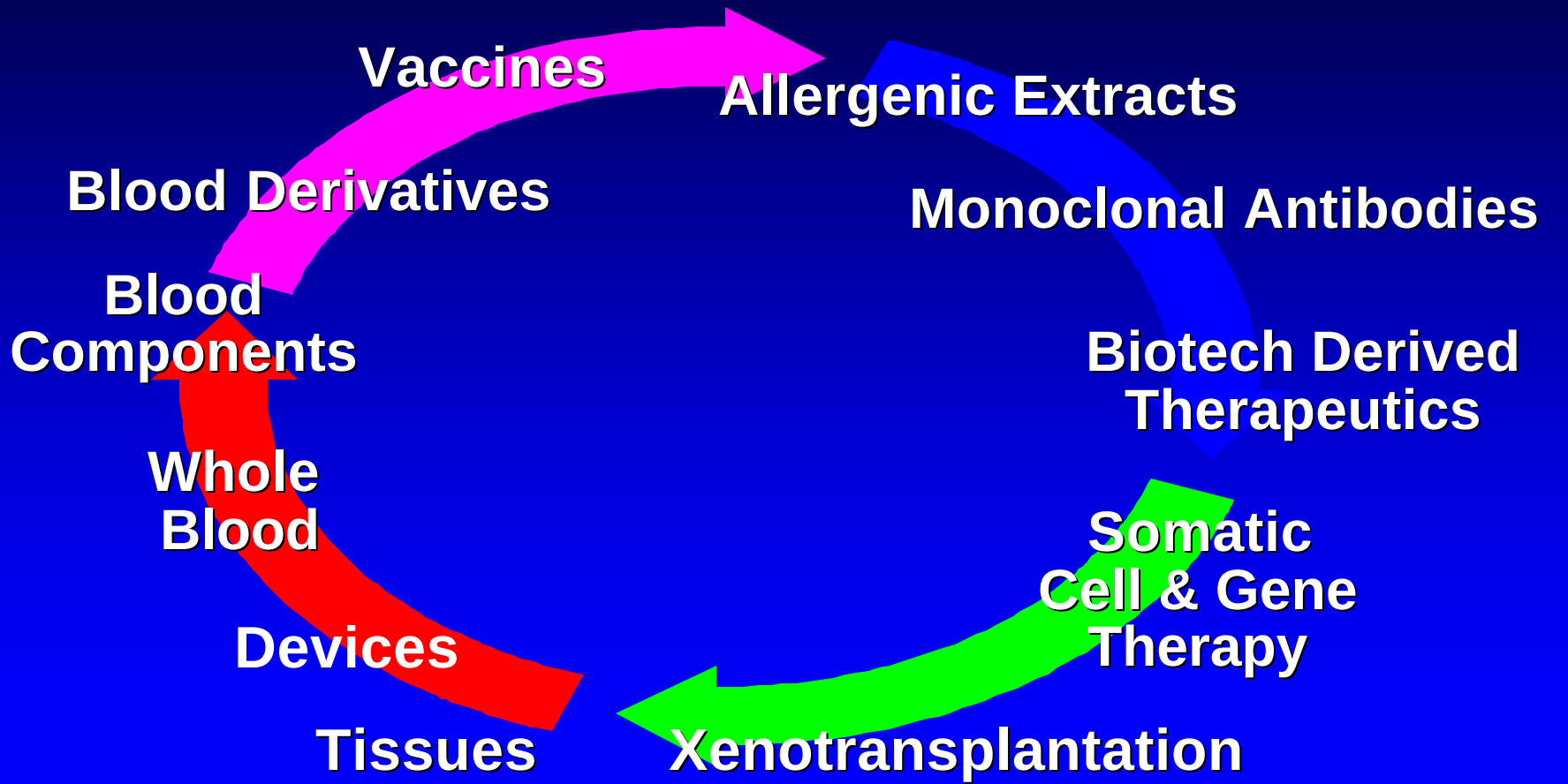
1988 — CBER

1992 — PDUFA

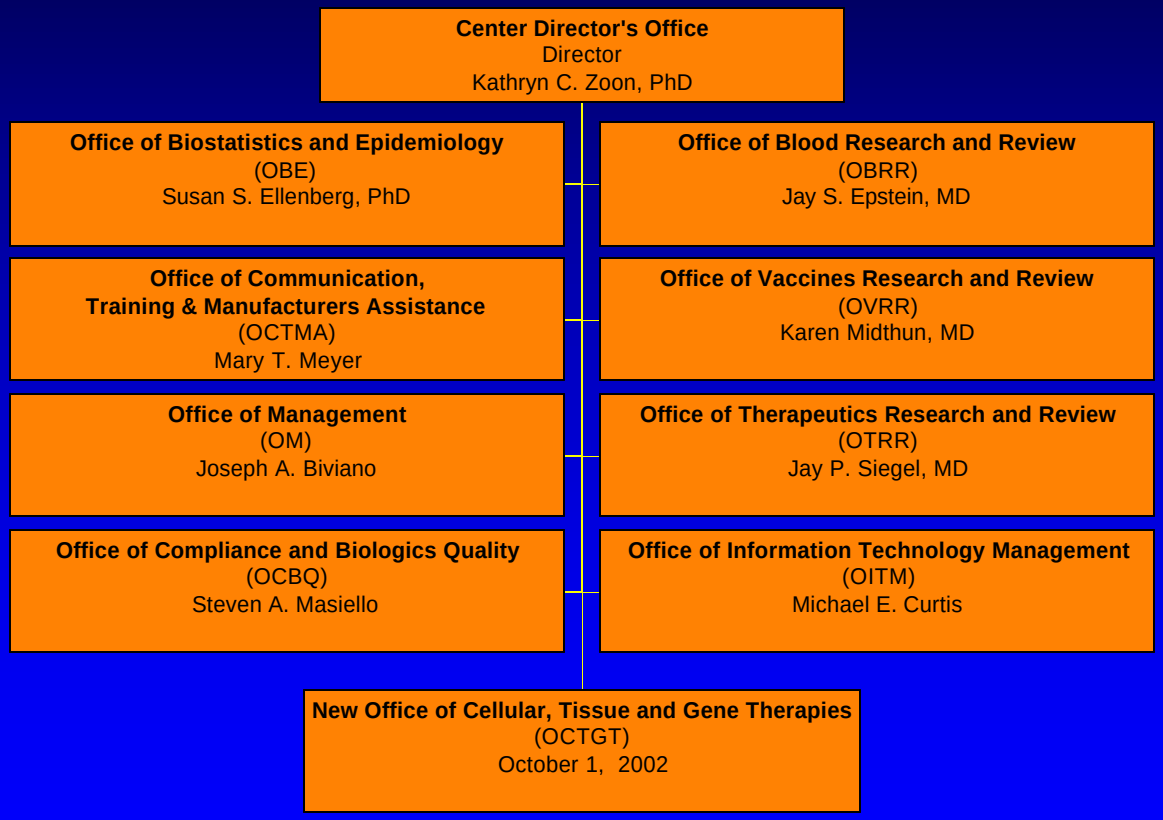
1997 — FDAMA

2002 — Future??

BIOLOGICAL PRODUCTS REGULATED BY CBER



CBER Organization

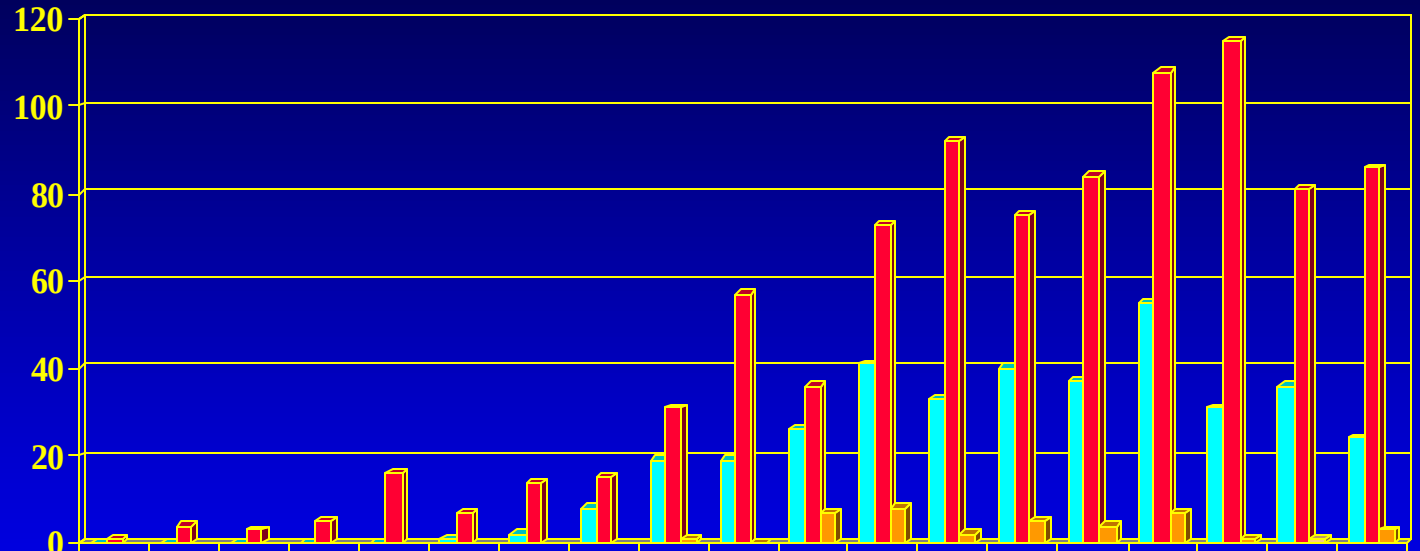


Office of Cellular, Tissue, and Gene Therapies (OCTGT)

Why?

- Increase in regulatory activities in the areas of cellular and tissue-based products, gene therapies, and all forms of stem cell transplantation.
- Consolidation of products into one office
  - Products getting more complex
  - New science advances
  - Need for seamless and transparent coordination and communication

Gene Therapy, Somatic Cell Therapy, Xenotransplantation INDs/IDEs
Received FY 1984 - FY 2002



	FY84	FY85	FY86	FY87	FY88	FY89	FY90	FY91	FY92	FY93	FY94	FY95	FY96	FY97	FY98	FY99	FY00	FY01	FY02
GT INDs	0	0	0	0	0	1	2	8	19	19	26	41	33	40	37	55	31	36	24
SCT INDs/IDEs	1	4	3	5	16	7	14	15	31	57	36	73	92	75	84	108	115	81	86
Xeno INDs									1	0	7	8	2	5	4	7	1	1	3

Note: A total of 7 INDs were for Xeno and GT, and are included in the counts for both.

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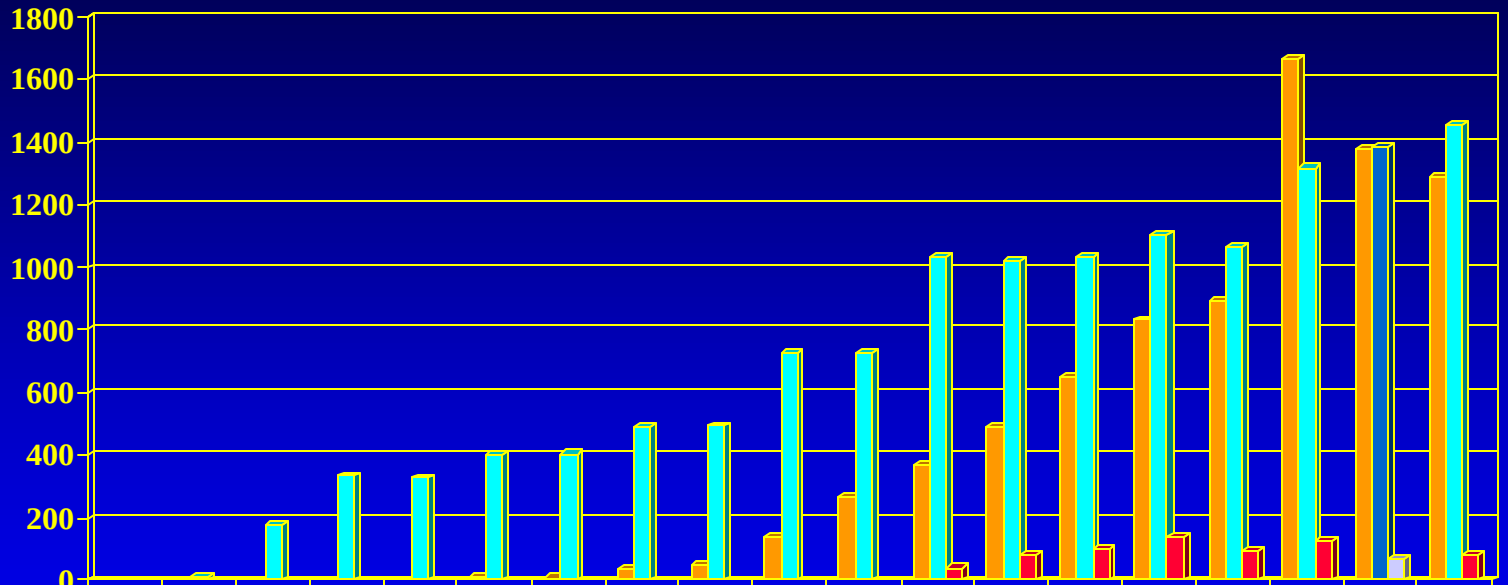
Gene Therapy, Somatic Cell Therapy, Xenotransplantation

IND/IDE Amendments

Received FY 1984 - FY 2002



	FY84	FY85	FY86	FY87	FY88	FY89	FY90	FY91	FY92	FY93	FY94	FY95	FY96	FY97	FY98	FY99	FY00	FY01	FY02
GT Amend's						13	12	40	54	137	268	369	488	650	834	892	1670	1378	1285
SCT Amend's	1	14	180	337	328	403	405	488	494	730	728	1033	1023	1036	1105	1068	1315	1386	1453
Xeno Amend's											3	43	82	103	139	96	124	68	82

Note: A total of 317Amendments were for INDs that are both Xeno and GT and are included in the counts for both..

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Mission

- Regulatory and review responsibilities:
  - Tissues
  - Cellular and Tissue-based products
  - Gene Therapies
  - Xenotransplantation
  - Unique assisted reproduction (ooplasm transfer)
  - Combination Products containing living cells/tissues
- Assure the safety, identity, purity, and potency of novel products

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Expertise

- Molecular and cell biology
- Viral and nonviral gene therapy vectors
- Nucleic acid chemistry
- Genomics
- Proteomics,
- Tissue and Organ Regeneration
- Developmental and Reproductive Biology
- Stem Cell Biology and Physiology
- Medical
- Pharmacology/Toxicology

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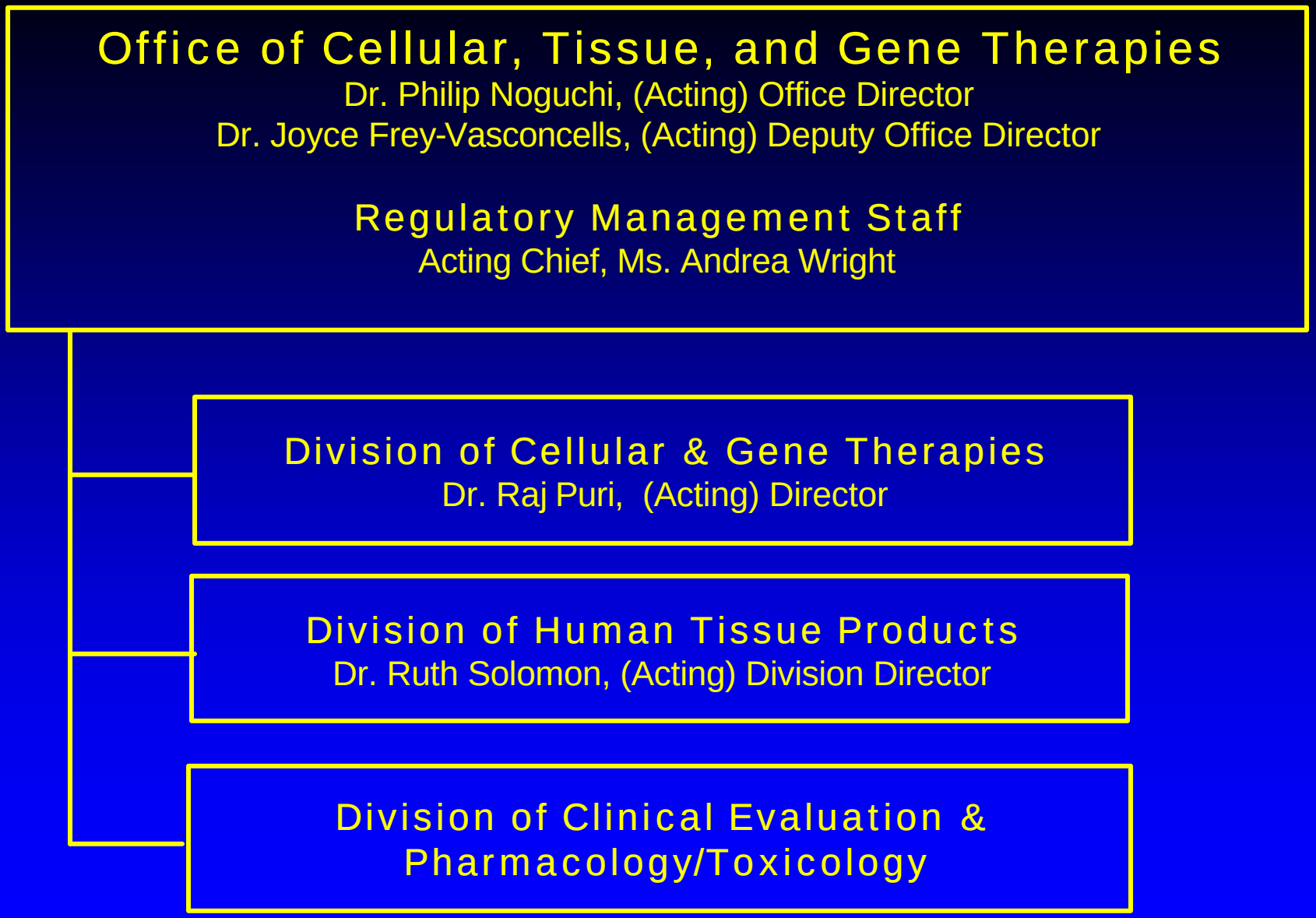
Office of Cellular, Tissue, and Gene Therapies
Dr. Philip Noguchi, (Acting) Office Director
Dr. Joyce Frey-Vasconcells, (Acting) Deputy Office Director
Regulatory Management Staff
Acting Chief, Ms. Andrea Wright
Division of Cellular & Gene Therapies
Dr. Raj Puri, (Acting) Director
Division of Human Tissue Products
Dr. Ruth Solomon, (Acting) Division Director
Division of Clinical Evaluation & Pharmacology/Toxicology

CBER Priorities FY 2003

- **Ensure the safety and efficacy of biological products while facilitating their development and meeting Prescription Drug User Fee Act (PDUFA) goals**
- **Ensure a strong science base supported by excellence in research that is directly targeted to the evaluation and regulation of biological products**

CBER Priorities FY 2003

- **Ensure the safety of, and public confidence in, the nation's blood supply and tissues**
- **Facilitate the development and approval of significant vaccine, blood and therapeutic products through review, policy formulation, regulation development, guidance issuance to industry, workshops and meetings**
- **Implement OC management initiatives, e.g. CBER/CDER product transfers as appropriate**

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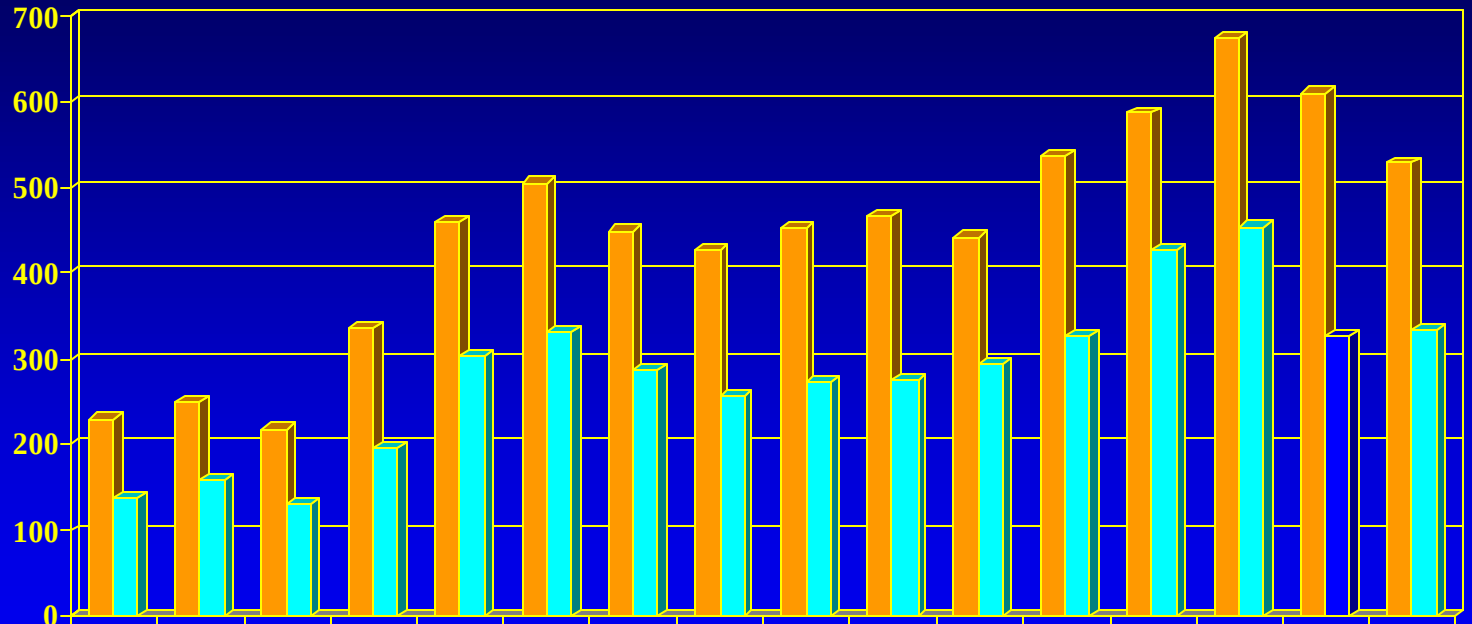
CBER Priorities FY 2003

- **Improve automated system to support the review and evaluation of biological products**
- **Implement New Office of Cellular, Tissue and Gene Therapy Products**
- **Develop effective measures for Counter Terrorism**
- **GMPs for the 21st Century**

CBER INDs/IDEs
Received FY 1987 - FY 2002



	FY87	FY88	FY89	FY90	FY91	FY92	FY93	FY94	FY95	FY96	FY97	FY98	FY99	FY00	FY01	FY02
Total INDs/IDEs Received	231	250	217	335	459	505	449	428	452	467	442	538	587	674	611	528
Biotech INDs/IDEs	138	159	131	196	304	331	288	257	273	275	295	327	427	453	326	333

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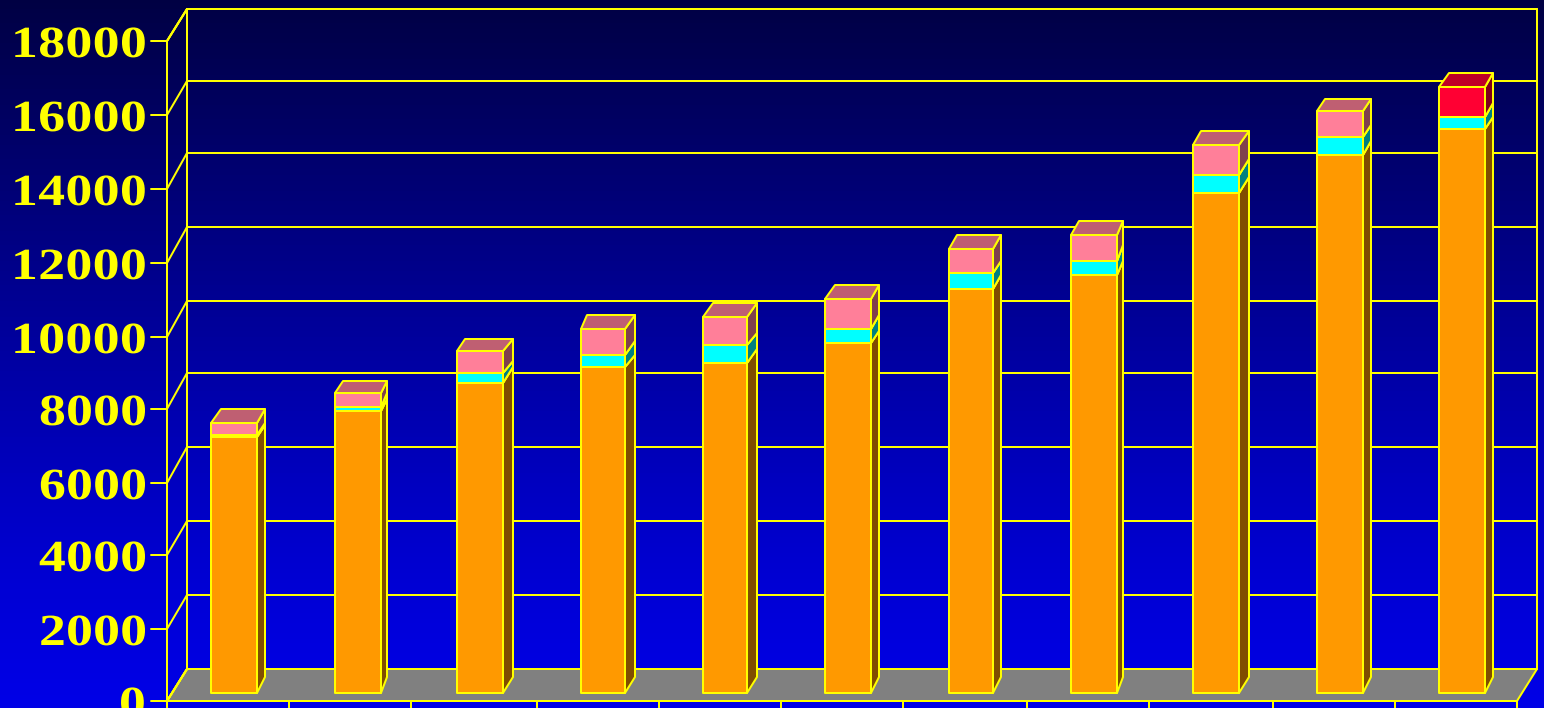
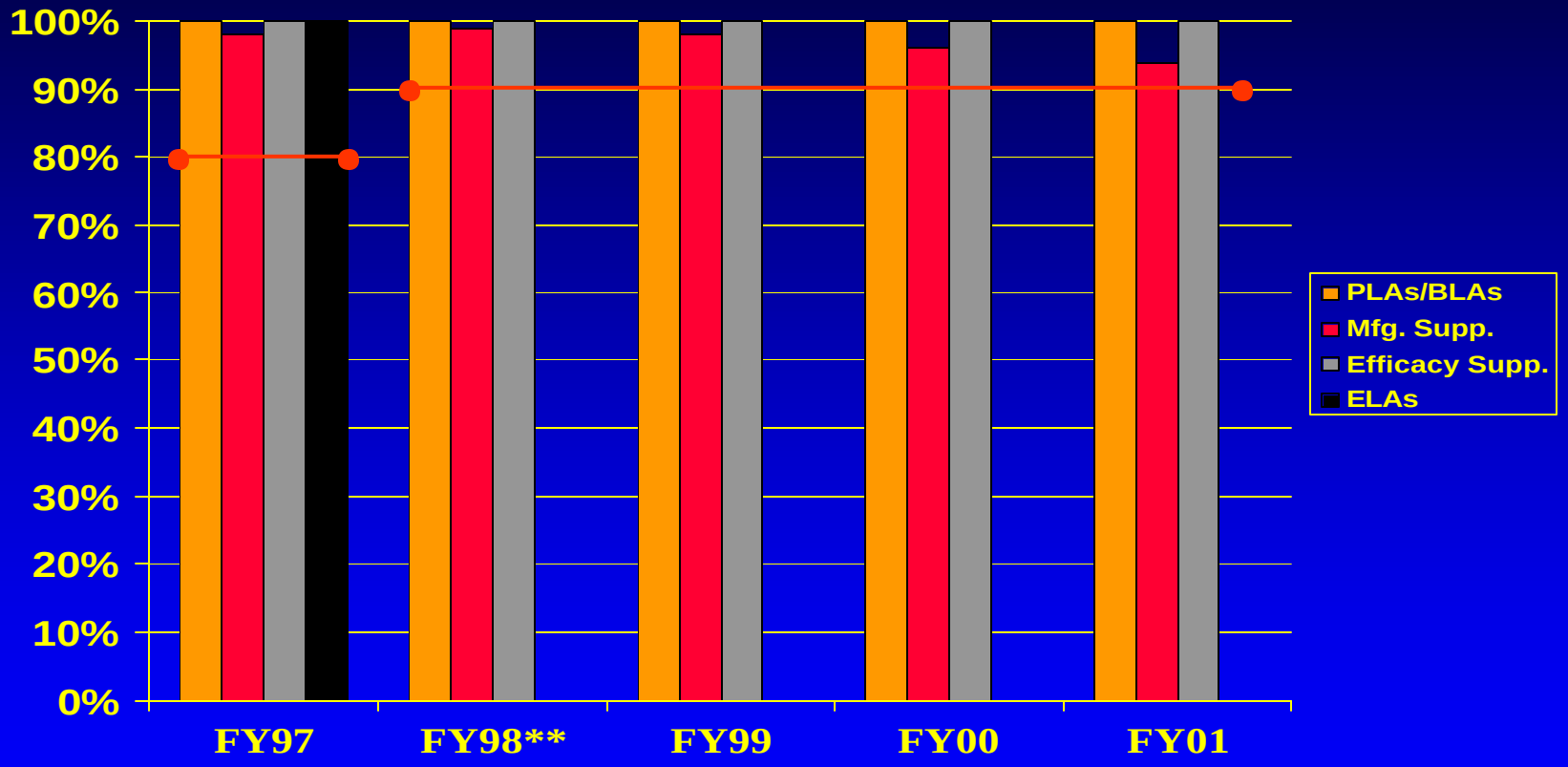
CBER IND/IDE/MF Amendments
Received FY92-FY02



	FY92	FY93	FY94	FY95	FY96	FY97	FY98	FY99	FY00	FY01	FY02
MFs	382	365	611	713	780	812	678	698	779	697	837
IDEs	54	130	210	375	457	431	397	386	516	480	355
INDs	6914	7628	8453	8827	8966	9479	10988	11371	13620	14628	15299

CBER User Fee Review Performance
License Applications and Supplements
% of First Actions Within Goal*
By Cohort Fiscal Years 1997-2001



* PDUFA Performance Goals: FY97 - FY01=90% (Indicated by Red Lines)
** Beginning in FY98 ELAs were no longer included in PDUFA goals

Data through 30 Sep 02; FY 01 is not yet complete.

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Other CBER Initiatives

- **Blood Action Plan**
- **Tissue Action Plan**
- **Xenotransplantation Action Plan**
- **Medical Device User Fee Program?**

Blood Action Plan Accomplishments

- **Updating Blood Regulations and Reinvention of Blood Regulation**

  Proposed and Final Rules Prepared : >14

  Public Workshops on Blood Issues : >23

  Guidances for Industry Developed : >22

- **Monitoring and Increasing the Blood Supply**

  The PHS Blood Safety Committee has developed a plan to address supply issues. It is being implemented under the FDA's Blood Action Plan

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Blood Action Plan Accomplishments

- **Emerging Infection**
  - Database of Potential Threats to the Blood Supply
  - Quarterly PHS meetings, e.g. West Nile Virus
- **Team Biologics**
  - Plasma Fractionation; *in Vitro* Diagnostics,
  - Blood and Plasma Collection
- **FDA Response to Emergencies**
  - CBER-wide training
  - Quarterly Performance Reviews

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Status of Tissue Regulations

- **Proposed Rule: Suitability Determination for Donors of Human Cellular and Tissue-Based Products (HCT/Ps) Pub: 9/30/99 (under revision)**
- **Proposed Rule: Good Tissue Practices: Inspection and Enforcement for Manufacturers of (HCT/Ps) Pub: 1/8/01**
- **Final Rule 21 CFR Part 1271 : Establishment Registration and Listing for (HCT/Ps) Pub: 1/19/01**

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Future Action

- FDA/AATB Liaison Meetings
- Public meetings and workshops as needed for reproductive tissues
- Improvements in Tissue Reference Group
- Issue Guidances as needed/Finalize Proposed Rules
- Advisory Committees
- DHHS Assisted Reproductive Technology (ART) Working Group

Xenotransplantation Initiatives

- Xenotransplantation Action Plan (XAP)
- Secretary's Advisory Committee on Xeno (SACX)
- Xeno Sub-Committee of the Biological Response Modifiers Advisory Committee (BRMAC)
- National Xenotransplantation Registry and Database

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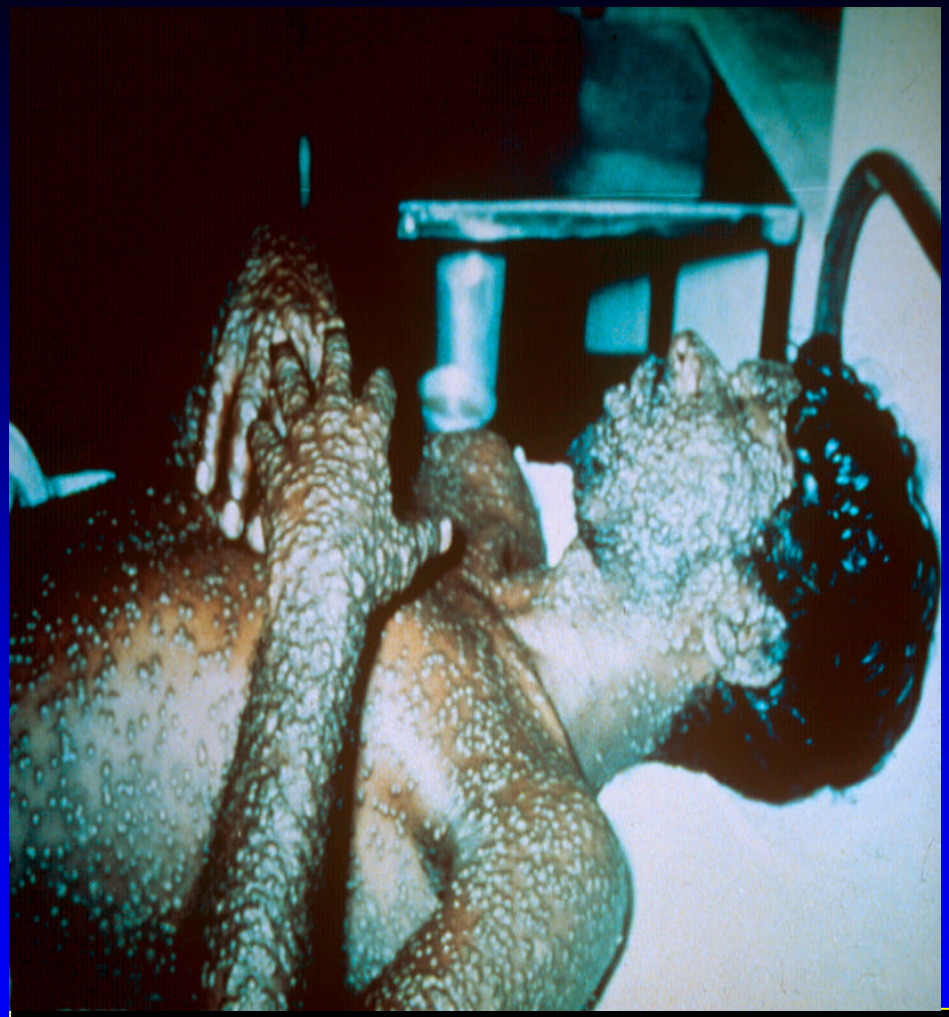

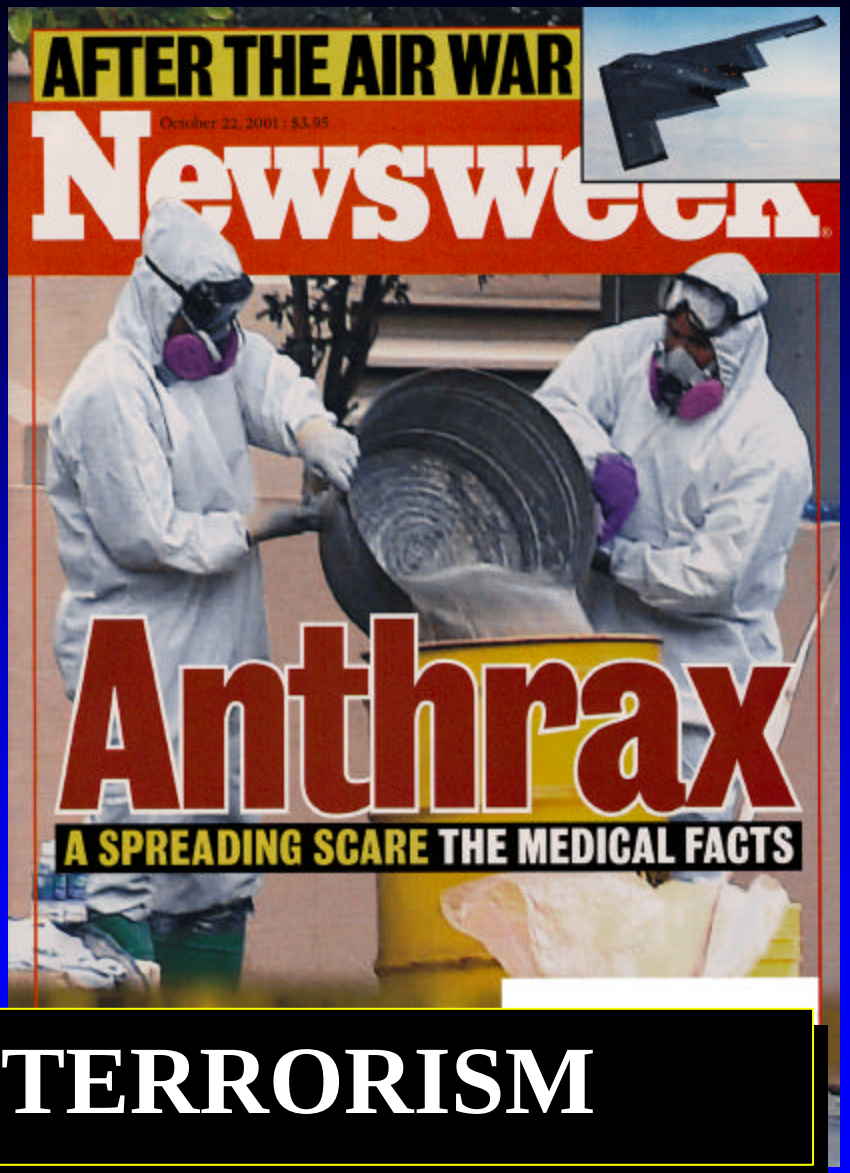

COUNTER- BIOTERRORISM

Countering Bioterrorism
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- Facilitate the availability of necessary medical products
- Scientific infrastructure to ensure availability of approved medical products
- Ensure availability of specialized equipment and facilities for containment
- Establish and disseminate the necessary guidance/standards

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Key Actions
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- Expedite development and licensure of new vaccines for anthrax, smallpox, and associated VIG
- Develop new approaches to approve medical products for countering bioterrorism
- Continue activities related to stockpile and product shortages
- Participate in numerous collaborative activities with other government agencies

HOW TO GET INFORMATION FROM CBER

Send E-MAIL to:

"CBER_INFO@CBER.FDA.GOV"

"OCTMA@CBER.FDA.GOV"

To visit CBER's Home page:

"www.fda.gov/cber"